

腹腔镜探查“华西四步法”在诊断胃癌腹膜转移中的应用及临床价值

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【摘要】 胃癌是全球常见的消化道恶性肿瘤之一,其以高发病率和高死亡率给社会带来了沉重负担。胃癌腹膜转移患者预后差,并且是胃癌患者复发转移的主要因素。临床上诊断胃癌腹膜转移主要依靠增强CT和PET-CT等方法,但这些方法对于精准检测微小腹膜转移病灶效果有限。目前,腹腔镜探查仍被认为是诊断胃癌腹膜转移最可靠的方法,其可在直视状态下探查原发灶、胃周淋巴结和腹膜转移的情况,并可同时获得组织学和细胞学标本以明确病理诊断。然而,壁腹膜和脏层腹膜构成的面积大、空间褶皱多,为尽可能地全面探查肿瘤及腹膜情况,笔者团队提出了“华西四步法”以规范腹腔镜探查操作流程。“华西四步法”除具有安全而简单易操作的优点外,可以达到全面探查腹腔的目的。本文主要阐述当前临床诊断胃癌腹膜转移面临的困难,并着重介绍腹腔镜探查“华西四步法”在诊断胃癌腹膜转移中的重要价值。

【关键词】 胃肿瘤; 腹膜转移; 腹腔镜探查; 华西四步法

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Application and clinical significance of the "Four-Step Procedure" of laparoscopic exploration in the diagnosis of gastric cancer with peritoneal metastasis

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【Abstract】 Gastric cancer is one of the most common malignant tumors of the digestive tract globally, causing a heavy burden on society due to its high incidence and mortality rates. Patients with gastric cancer and peritoneal metastasis suffer poor prognosis, and peritoneal metastasis is a major factor in the recurrence and metastasis of gastric cancer. Currently, the diagnosis of peritoneal metastasis mainly relies on contrast-enhanced CT, PET-CT, and other imaging techniques, but these technologies have a limited capability to detect small lesion of peritoneal metastases. Laparoscopic exploration is still considered as the most reliable method to diagnose peritoneal metastasis of gastric cancer. It allows direct visualization of the abdominal cavity and peritoneal regions, facilitating the detection of metastases. Furthermore, it enables the collection of histological or cytological specimens for definitive pathological diagnosis. However, the area formed by the parietal peritoneum and visceral peritoneum is large and has many folds in space. To explore the tumor and peritoneum as comprehensively as possible, our team has proposed the "Four-Step Procedure" of laparoscopic exploration for gastric cancer to standardize the operation process of

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laparoscopic exploration, which is characterized by its safety, comprehensiveness, precision and ease of implementation. This article primarily discusses the limitation of routine clinical techniques in diagnosing peritoneal metastasis in gastric cancer and introduce the significant value of the "Four-Step Procedure" in diagnosing peritoneal metastasis in gastric cancer.

【Key words】 Stomach neoplasms; Peritoneal metastasis; Laparoscopic exploration; Four-Step procedure

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胃癌是全球最常见的消化系统恶性肿瘤之一,其发病率和死亡率分别位居我国第5位和第3位^[1]。胃癌以其高发病率和高死亡率,给社会带来沉重负担。胃癌在东亚地区,尤其是日本、韩国和中国发病率位居全球前列,而东欧及北美地区发病率较低^[2]。目前,针对胃癌的治疗模式仍以根治性手术切除为主,辅以化疗、放疗、免疫治疗和靶向治疗等综合治疗。

由于我国目前胃镜筛查并未大规模普及,而早期胃癌缺乏特异性临床症状,加之普通群众对胃癌早诊早治的意识不强,我国大部分胃癌患者确诊时即为进展期,预后较差。文献报道,10%~15%的胃癌患者在确诊时存在腹膜转移,无法行手术切除^[3-6]。腹膜是胃癌患者最常见的转移部位之一。既往研究结果显示,存在腹膜转移的胃癌患者,其T分期更晚,分化程度更低,肿瘤侵犯淋巴管及血管的比例更高,预后更差,平均中位生存时间<1年,成为胃癌患者死亡的主要原因之一^[7-8]。

随着医学技术的发展,胃癌的诊疗模式逐渐向个体化和精准化方向转变。准确全面地评估患者肿瘤分期,包括原发病灶情况、胃周组织侵犯情况、胃周或远处淋巴结转移情况、脏器转移和腹膜转移等情况,对制定个体化的治疗决策至关重要。目前,术前新辅助治疗能够明显改善局部进展期胃癌患者的长期预后^[9-12]。这更需要我们准确判断患者的分期,特别是不容易准确诊断而发病率又比较高的胃癌腹膜转移。针对临床诊断为进展期或晚期的胃癌患者进行腹腔镜探查,能够弥补影像学检查的不足,进一步准确评估患者肿瘤分期及腹膜转移情况,为患者提供个体化的术前新辅助治疗、转化治疗或姑息性治疗的依据,改善患者整体预后。笔者团队前期针对胃癌腹膜转移开展了深入研究,并针对如何规范化开展腹腔镜探查提出了“华西四步法”操作流程,以提高腹膜转移诊断准确性。

本文将阐述临床常用技术在胃癌腹膜转移诊断中的应用和面临的困难,并着重介绍腹腔镜探查

“华西四步法”在胃癌腹膜转移中的临床价值。

一、术前常规检查方法诊断胃癌腹膜转移的现状 & 局限性

如何尽早发现并诊断胃癌患者存在腹膜转移,是我们关注的重点之一。腹部超声、尤其是超声造影在检测肿瘤肝转移方面敏感性较高,准确率为53%~76%^[13]。但其对腹膜转移的检测敏感性较差,故临床实践中基本不采用其作为腹膜转移的诊断工具。

目前,增强CT和PET-CT等是常用于术前胃癌患者是否存在腹膜转移的检查方法。腹部增强CT在评估原发肿瘤大小、形态、部位、浸润深度、邻近脏器侵犯、淋巴结转移及远处转移等方面具有优势,但其对腹膜转移、尤其是微小腹膜转移灶的检出能力较差。CT预测的腹膜转移准确率在75%~83%之间,常见的CT表现有腹腔积液、腹膜结节状增厚或局部粘连成饼状等表现;有10%~30%的患者术前CT等检查未发现腹膜转移,但却在手术中或腹腔镜探查中发现存在腹膜转移,即隐匿性腹膜转移^[14-16]。PET-CT对胃癌患者腹膜转移检出准确度更高^[17]。一项回顾性研究结果显示,CT和PET-CT对胃癌腹膜转移的检查特异度分别为91.6%和98.9% ($P=0.035$)^[18]。但由于PET-CT价格昂贵,并未常规用于胃癌患者腹膜转移的筛查。此外,黏液腺癌或印戒细胞癌等特殊类型的胃癌对¹⁸氟-氟代脱氧葡萄糖(¹⁸F-FDG)的摄取能力低,因此,基于¹⁸F-FDG的PET-CT不适用于此种类型的胃癌患者的检测^[19]。近年,新型的基于⁶⁸GA-FAPI的PET-CT已应用于临床,并发现其在诊断胃癌腹膜转移中具有较好的敏感性和特异性。研究显示,⁶⁸GA-FAPI PET-CT针对胃癌肿瘤原发病灶及远处转移、腹膜转移及淋巴结转移等方面,均优于¹⁸F-FDG PET-CT^[20-21]。

血清学肿瘤标志物与患者肿瘤的浸润程度、有无转移及预后相关^[22-23]。既往研究结果显示,伴有腹膜转移的胃癌患者CEA、CA125、CA19-9的表达水平较高^[24]。CA125在预测胃癌腹膜转移方面具

有较高的应用价值,且CA125在伴有腹水脱落细胞学阳性的患者中表达量更高^[25-27]。有学者研究结果显示,血清CA125在预测胃癌腹膜转移方面具有高特异度(96.5%)和高准确率(92.8%)的特点,但其灵敏度为43.6%^[28]。CA72-4被认为与胃癌的临床分期高度相关,且与胃癌患者的复发和转移相关^[29]。其在预测胃癌腹膜转移方面具有一定的应用价值。但整体而言,血清学肿瘤标志物的灵敏度均较低,在临床实践中用于诊断胃癌腹膜转移的价值有限。

近年来,随着人工智能技术、生物大数据及影像组学的快速发展,有研究者将这些多源异构临床诊疗数据通过人工智能技术加以整合,以获得更优的无创性胃癌腹膜转移诊断模型^[30]。但在现阶段,这些模型的稳定性和扩展性仍有局限性,在临床应用中尚不成熟。

二、腹腔镜探查在胃癌腹膜转移中的应用

腹腔镜探查弥补了术前影像学或血液学检查的不足,能够直观地检测到是否存在腹膜转移。1984年,Gross等^[31]首次报道了腹腔镜探查技术用于评估胃癌临床分期。腹腔镜探查被越来越多地用于胃癌、胰腺癌和妇科肿瘤等多种实体肿瘤临床分期的评估及腹膜转移的判断中^[32]。这对制定肿瘤患者后续治疗方案的决策十分重要。Possik等^[33]为360例胃癌患者进行了腹腔镜探查,其结果显示,腹腔镜探查技术在判断胃癌腹膜转移方面有着良好的使用价值。一项腹腔镜、超声和CT对癌症分期中的前瞻性比较结果显示,在探查腹膜和肝脏表面微小转移灶方面,腹腔镜较影像学检查更为敏感^[34]。有研究表明,腹腔镜探查在诊断胃癌腹膜转移方面比CT、PET-CT和超声检查更优^[34-37]。既往一篇荟萃分析结果显示,腹腔镜探查在胃癌腹膜转移的诊断中具有100%的特异度,而灵敏度则为84.6%^[38]。

腹腔镜探查目前被认为是诊断胃癌腹膜转移最可靠的方法,其具有切口小、出血量少、创伤小和术后住院时间短的优点,尤其适用于术前怀疑存在腹膜转移的病例^[19]。在腹腔镜技术的辅助下,术者通过腹腔镜可以在直视下进行全面且细致的腹腔探查,检查腹膜是否存在转移病灶,评估胃癌腹膜转移的分布及严重程度,以及判断胃癌的可切除性。此外,腹腔镜探查术中可以对可疑腹膜转移病灶行组织病理活检,收集腹水或腹腔灌洗液进行脱

落细胞学检查,以获得组织学或细胞学病理证据,为患者后续治疗方案的制定提供依据。

腹腔镜探查主要目的是评估肿瘤分期及有无转移,避免不必要的非治疗性剖腹手术,实现术前精准临床分期以制定个性化的精准治疗方案。研究表明,腹腔镜探查可以降低非治疗性剖腹手术的比例及手术相关并发症的发生率^[39];腹腔镜探查术后有30.0%~55.7%的胃癌患者改变了原本手术切除的治疗策略^[40-41]。

既往研究结果显示,针对cT3~4N0/+M0、低分化腺癌、BormannⅢ~Ⅳ型、皮革胃及合并腹水的患者,应积极进行腹腔镜探查,且腹水是胃癌腹膜转移的独立危险因素^[11,42-43]。日本《胃癌治疗指南》及《腹膜播散诊疗指南(2021版)》均推荐,应针对存在上述危险因素的胃癌腹膜转移高风险人群进行腹腔镜探查^[44-45]。欧洲医学肿瘤学会(European Society of Medical Oncology,ESMO)和美国国立综合癌症网络(National Comprehensive Cancer Network,NCCN)的诊疗指南也均建议,针对可切除的局部进展期胃癌患者进行腹腔镜探查^[46-47]。结合笔者团队的临床实践,我们认为,对于T3~4期胃癌推荐行腹腔镜探查。

三、腹腔镜探查“华西四步法”在诊断胃癌腹膜转移中的应用及临床价值

腹腔内部空间大,腹膜表面积大、褶皱多且内脏器官众多,全面而细致地进行探查,是保证腹腔镜探查质量的关键。一套全面而规范的腹腔镜探查流程,在保证探查质量和避免遗漏方面尤为重要。笔者团队于2016年起,针对局部进展期胃癌患者,严格按照“华西四步法”全面且细致地进行了腹腔镜探查,结果显示,腹腔镜探查“华西四步法”具有安全可靠、简单易学和全面细致的优点^[48]。尤其可以指导探查经验较为欠缺的医生、或刚接触腹腔镜探查手术的年轻医生来开展这项技术,对保证腹腔镜探查质量、提高诊断胃癌腹膜转移的准确率及提高胃癌诊治水平,尤为重要。腹腔镜探查“华西四步法”简要操作步骤如下^[49]。

1. 探查前腹壁及腹部脏器表面:患者取仰卧位,按照顺时针方向和“O”形路线,依次探查双侧膈顶、肝圆韧带、镰状韧带及前腹壁。按照“S”形路线,依次探查肝脏、横结肠、左侧腹壁、左结肠旁沟、降结肠肠管、下腹壁、小肠肠管、右侧腹壁、右结肠旁沟和升结肠肠管。

2.探查盆腔及腹部脏器表面:患者取头低脚高位,依次探查盆腔及腹部脏器表面,重点关注双侧髂窝、膀胱底及腹膜反折部位;女性患者还应关注双侧附件及子宫底有无可疑病灶。

3.探查肠系膜及小肠:患者恢复仰卧位或取头高脚低位,探查横结肠及小肠系膜和系膜根部。

4.探查胃及胃周:患者保持仰卧位,探查胃原发病灶及胃周受累情况,关注小网膜及肝肾隐窝等邻近结构有无肿瘤侵犯。

腹腔镜探查“华西四步法”操作流程简单方便,操作时间短,易操作^[49]。有研究表明,腹腔镜探查过程中,小肠系膜、横结肠及网膜囊容易在探查时被忽略^[34]。而腹腔镜探查“华西四步法”探查了以上易于被忽略的位置,结合腹腔镜具有局部放大手术视野的优势,许多可疑的微小腹膜转移灶也可以被发现,这无疑提高了腹腔镜探查的准确性,降低了假阴性率。

笔者团队收集了 409 例接受腹腔镜探查“华西四步法”的胃癌患者临床数据及病理资料,结果显示,65 例存在腹膜转移和(或)腹腔脱落细胞学阳性;分层分析结果显示,cT3 和 cT4 期患者中分别有 7 例(7.4%)和 55 例(27.9%)存在腹膜转移和(或)腹腔脱落细胞学阳性;腹腔镜探查后,168 例患者接受了腹腔镜胃切除术,35 例接受了开腹手术,143 例接受了新辅助化疗,63 例接受了转化治疗^[43]。这使得部分患者避免了非治疗性的剖腹探查手术,及时接受新辅助化疗或姑息性化疗,改善了患者的预后。既往研究结果显示,腹腔镜探查术能够在 13.0%~22.6% 的局部进展期胃癌患者、尤其是 T4 期患者中发现腹膜转移^[36,50-53]。分析笔者团队腹腔镜探查阳性比例较高的原因,可能为“华西四步法”具有更规范、细致且全面的探查顺序及操作步骤,并且全部收集了腹腔冲洗液或腹水以完善病理学检查。这显示腹腔镜探查“华西四步法”在检出腹膜转移方面是可靠的。

腹腔镜探查避免了患者因不必要的非治疗性剖腹手术导致住院时间延长和化疗的延迟。本中心接受“华西四步法”探查术后患者平均住院日为 5 d,包括第 1 周期化疗,并未明显延长术后住院日;腹腔镜探查手术的并发症发生率很低,为 0.6%~5.1%,其中最多见的并发症是腹腔内脏器源性损伤、出血和感染^[40,42]。本中心 207 例行单纯腹腔镜探查“华西四步法”的患者其术后并发症发生

率为 2.9%,其中术后肺部感染 4 例,尿潴留 2 例^[43]。这提示腹腔镜探查“华西四步法”是安全可行的。

综上所述,伴有腹膜转移的胃癌患者预后不佳,如何尽早地发现腹膜转移对每例胃癌患者来说至关重要。术前影像学 and 血液学检查方法虽然无创,但因其具有的局限性不利于精准诊断胃癌腹膜转移。腹腔镜探查技术具有创伤小、手术时间短、操作简单及术后并发症少等优点,其腹膜转移诊断准确率优于影像学检查。腹腔镜探查“华西四步法”在常规腹膜探查技术基础上做了提升和改进,形成了一套全面且规范的腹腔镜探查技术流程,具有安全可靠、全面细致、简单易操作的优点,在胃癌腹膜转移诊断方面有极大的应用价值,有助于提升腹腔镜探查质量,提高胃癌诊疗水平。随着人工智能和医学大数据等新技术、新理念的发展融合,创造一种精准的胃癌腹膜转移无创诊断技术仍是我们努力的方向。

利益冲突 所有作者均声明不存在利益冲突

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